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EXAMINER	
GOLLAMUDI, SHARMILA S	

ART UNIT	PAPER NUMBER
1616	

DATE MAILED: 11/14/2006

Please find below and/or attached an Office communication concerning this application or proceeding.

Office Action Summary	Application No.	Applicant(s)	
	09/914,795	BERNDL ET AL.	
	Examiner	Art Unit	
	Sharmila S. Gollamudi	1616	

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) OR THIRTY (30) DAYS, WHICHEVER IS LONGER, FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133). Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

1)☒ Responsive to communication(s) filed on *24 August 2006*.

2a)☒ This action is **FINAL**. 2b)☐ This action is non-final.

3)☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

4)☒ Claim(s) *2-18* is/are pending in the application.

4a) Of the above claim(s) _____ is/are withdrawn from consideration.

5)☐ Claim(s) _____ is/are allowed.

6)☒ Claim(s) *2-18* is/are rejected.

7)☐ Claim(s) _____ is/are objected to.

8)☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

9)☐ The specification is objected to by the Examiner.

10)☐ The drawing(s) filed on _____ is/are: a)☐ accepted or b)☐ objected to by the Examiner.

Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).

Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).

11)☐ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

Priority under 35 U.S.C. § 119

12)☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).

a)☐ All b)☐ Some * c)☐ None of:

1.☐ Certified copies of the priority documents have been received.

2.☐ Certified copies of the priority documents have been received in Application No. _____.

3.☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

Attachment(s)

1) ☐ Notice of References Cited (PTO-892)
2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
3) ☐ Information Disclosure Statement(s) (PTO/SB/08) Paper No(s)/Mail Date _____.
4) ☐ Interview Summary (PTO-413) Paper No(s)/Mail Date. _____.
5) ☐ Notice of Informal Patent Application
6) ☐ Other: _____.

DETAILED ACTION

Receipt of Remarks and Amendments filed 8/24/06 is acknowledged. Claims **2-18** are pending in this application. Claim 1 stands cancelled.

New Grounds of Rejections Necessitated by Amendments

Claim Rejections - 35 USC § 112

The following is a quotation of the second paragraph of 35 U.S.C. 112:

> The specification shall conclude with one or more claims particularly pointing out and distinctly claiming the subject matter which the applicant regards as his invention.

Claims 2-10 and 12-18 are rejected under 35 U.S.C. 112, second paragraph, as being indefinite for failing to particularly point out and distinctly claim the subject matter which applicant regards as the invention.

Independent claim 8 is directed to a process of making a solid dosage form comprising 0.5 to 25% of by weight of the at least one active ingredient, 0.5 to 60% by weight of the at least one cyclodextrin, 50 to 98% by weight of the at least one polymeric binder, and • 0 to 50% by weight excipients. There is insufficient antecedent basis for "the at least one" limitation in the claim.

Dependent claim 12 is directed to a solid dosage form comprising 0.5 to 25% of by weight of the at least one active ingredient, 0.5 to 60% by weight of the at least one cyclodextrin, 50 to 98% by weight of the at least one polymeric binder, and • 0 to 50% by weight excipients. There is insufficient antecedent basis for "the at least one..." limitation in the claim.

Claim 13 recites the limitation "said active ingredient" in line 1. There is insufficient antecedent basis for this limitation in the claim.

Claim 14 recites the limitation "said at least one cyclodextrin" in 1. There is insufficient antecedent basis for this limitation in the claim.

Claim 15 recites the limitation "said at least one cyclodextrin" in 1. There is insufficient antecedent basis for this limitation in the claim.

Claim 16 recites the limitation "said at least one polymeric binder" in 1. There is insufficient antecedent basis for this limitation in the claim.

Claim 17 recites the limitation "said at least one polymeric binder" in 1. There is insufficient antecedent basis for this limitation in the claim.

Claim 18 recites the limitation "said at least one polymeric binder" in 1. There is insufficient antecedent basis for this limitation in the claim.

Claim Rejections - 35 USC § 102

The following is a quotation of the appropriate paragraphs of 35 U.S.C. 102 that form the basis for the rejections under this section made in this Office action:

> A person shall be entitled to a patent unless –
>
> (b) the invention was patented or described in a printed publication in this or a foreign country or in public use or on sale in this country, more than one year prior to the date of application for patent in the United States.

Claims 2, 5-8, 11-14, and 17-18 are rejected under 35 U.S.C. 102(b) as being anticipated by EP 0564945. The rejection of claims 3-4 is withdrawn.

EP discloses a method of controlling insects. Example 3 discloses a process wherein 20 parts cyfluthrin, 0.1 parts triadminenol, 80 parts beta-cyclodextrin, 150 parts of a polymeric material Biopol (reads on polymeric binder), and 50 parts Carbowax 20M (also reads on polymeric binder-PEG water-soluble binder), are homogenized in an extruder at a temperature of 160°Celsius and then injection molded to a shaped form. Note Biopol is utilized in an amount of

about 50% and Carbowax in an amount of about 16.6%; thus the total polymeric binder is about 66%. With regard to claim 6, it is noted that the active and cyclodextrin implicitly form a complex during the process of melting the components and the reference does not explicitly state that the active and cyclodextrin are maintained in a uncomplexed state.

With regard to claim 7, it is the examiner's position that EP would have the same functional property since the devices are substantially similar and thus the properties must be the same. See MPEP2112 IV, V and 2112.01.

Response to Arguments

Applicant argues that claim 8 was not rejected and claims 2-7 have been amended to depend on claim 8. Thus, it is argued that the claims are not anticipated.

Applicant's arguments filed 8/24/06 have been fully considered but they are not persuasive. Firstly, the examiner points out that cancelled claim 1 which required 15-98% of a specific binder selected from PEG with a molecular weight of 4000, PVP, or copolymers comprising N-vinylpyrollidone and vinyl acetate. EP only taught about 16% of the claimed binder, PEG (Carbowax); thus the examiner could not reject dependent claim 8, which required 50-98% of the above binders recited in a Markush group. However, applicant has cancelled claim 1 and has amended claim 8 to be an independent claim. Claim 8 as amended only requires 50-98% of *at least one* polymeric binder without specifying the binder. Thus, claim 8 is a broader claim since cancelled claim 1 required a specific binder from a Markush group. Thus, the examiner has rejected claim 8 since EP teaches 50% of Biopol, which also reads on a polymeric binder. Further, the combination of Carbowax, which is also a binder, and Biopol

provide a weight percent of 66%. The examiner retains the right to go final since the amendment to claim 8 necessitated the new rejection.

Upon further consideration, the rejection of claims 3-4 has been withdrawn. With regard to claim 6, the process would implicitly cause the active agent and the cyclodextrin to complex and since EP does not specify that the cyclodextrin and active are prevented from complexing. As noted in the arguments of 3/31/03 the process causes the cyclodextrin and active to be complexed. Applicant has not argued the examiner's position and thus EP reads on this claim. With regard to claim 7, it is noted that applicant has not argued the examiner's position that the functional properties are inherent since the composition are substantially identical. Thus, the rejection is maintained.

> (e) the invention was described in (1) an application for patent, published under section 122(b), by another filed in the United States before the invention by the applicant for patent or (2) a patent granted on an application for patent by another filed in the United States before the invention by the applicant for patent, except that an international application filed under the treaty defined in section 351(a) shall have the effects for purposes of this subsection of an application filed in the United States only if the international application designated the United States and was published under Article 21(2) of such treaty in the English language.

Claims 5-7, 11-12, 14, 16-18 are rejected under 35 U.S.C. 102(e) as being anticipated by Stella et al (6,046,177).

Stella et al disclose a controlled release device comprising 5% of prednisone; 35% SAE-β-CD; 50% HPMC (modified natural polymeric binder as defined by page 4 of the specification); and 10% lactose (excipient). See column 18, lines 27-35. Example 4 discloses a solid dosage form comprising 25mg of an active, 300 mg of SAE-CD, 160mg EMDEX (dextrate binder-soluble), 20mg polyethylene oxide (synthetic binder), magnesium stearate, and corn starch.

It is noted that claim 5 is a product-by-process claim, however "even though product by process claims are limited by and defined by the process, determination of patentability is based on the product itself. The patentability of a product does not depend on its method of

production, If the product in the product-by-process claim is the same or obvious from a product of the prior art, the claim is unpatentable even though the prior art was made by a different process." *In re Thorpe*, 777 F.2d 695, 698, 227 USPQ 964, 966 (Fed.Cir. 1985).

With regard to claim 6, Stella discloses although the solid dosage form comprises the SAE-CD wherein majority of the therapeutic compound is not complexed, however the complex may form unintentionally during preparation of the solid dosage form. See column 11, lines 49-57. Stella discloses, at least 50% is not complexed, preferably at least 75% is not complexed; even more preferable at least 90% is not complexed; and the most preferable wherein at least 95% is not complexed. See column 12, lines 9-25. Thus, in the embodiment wherein at least 50% is not complexed, 50% would be complexed. In the embodiment wherein at least 75% is not complexed, 25% would be complexed. In the embodiment wherein at least 90% is not complexed, 10% would be complexed.

With regard to claim 7, it is the examiner's position that EP would have the same functional property since the devices are substantially identical; thus the properties must be the same. Further, it appears that in Figure 20, at least 18% is released in after 20 minutes. Thus, the burden has shifted to applicant to provide otherwise. See MPEP2112 IV, V and 2112.01.

Claims 11, 14-15, and 17 are rejected under 35 U.S.C. 102(e) as being anticipated by Baert et al (6,365,188).

Baert et al disclose a solid dosage form comprising 480mg of a hydroxypropyl-β-cyclodextrin and active agent extrudate in a ratio of 1:3 (about 18.8% active and about 37.6% cyclodextrin); about 26% microcrystalline cellulose; about 0.35% aerosol; about 0.58% magnesium stearate; and about 16.9% crospovidone (insoluble synthetic polymeric binder).

Claim Rejections - 35 USC § 103

The following is a quotation of 35 U.S.C. 103(a) which forms the basis for all obviousness rejections set forth in this Office action:

> (a) A patent may not be obtained though the invention is not identically disclosed or described as set forth in section 102 of this title, if the differences between the subject matter sought to be patented and the prior art are such that the subject matter as a whole would have been obvious at the time the invention was made to a person having ordinary skill in the art to which said subject matter pertains. Patentability shall not be negatived by the manner in which the invention was made.

The factual inquiries set forth in *Graham* **v.** *John Deere Co.*, 383 U.S. 1, 148 USPQ 459 (1966), that are applied for establishing a background for determining obviousness under 35 U.S.C. 103(a) are summarized as follows:

1. Determining the scope and contents of the prior art.
2. Ascertaining the differences between the prior art and the claims at issue.
3. Resolving the level of ordinary skill in the pertinent art.
4. Considering objective evidence present in the application indicating obviousness or nonobviousness.

Claims 2, 8-10, 13 are rejected under 35 U.S.C. 103(a) as being unpatentable over Stella et al (6,046,177).

As set forth above, Stella et al disclose a controlled release composition comprising 5% of prednisone; 35% SAE-CD; 50% HPMC (polymeric binder); and lactose (excipient). See column 18, lines 27-35. Stella teaches release rate modifiers include HPMC, HPC, cellulose acetate butyrate, cellulose acetate propionate, cellulose propionate, carrageenan, cellulose acetate, cellulose nitrate, methylcellulose, hydroxyethyl cellulose, ethylcellulose, polyvinyl acetate, latex dispersions, acacia, tragacanth, guar gum, and gelatin. See column 39, lines 10-20.

Stella et al teach a controlled release pharmaceutical composition comprising sulfoalkyl ether cyclodextrin. See abstract. Stella teaches the use of a rate release modifier to manipulate the release rate of the composition. Stella teaches the amount of the release rate modifier, i.e.

HPMC, depends on the release rate and the greater the amount of HPMC, the slower the release. For instance, a ratio of release rate modifier:drug may be 10:1 wherein the rate of release of the drug is greatly reduced compared to a ratio of 5:1. see column 17, lines 35-60.

Stella teaches one embodiment wherein the release of drug from the controlled release formulation of the invention is dependent upon the ratio of drug/cyclodextrin wherein the smaller the ratio, the faster the drug release and the larger the ratio, the slower the drug release from the formulation of the invention. See column 1, lines 60-65. Stella teaches the ratio of therapeutic agent:SAE-CD present in the complex can vary and can be in the range of about 1:2 to about 2:1, on a molar basis, respectively, and about 1:1. In another embodiment of the dosage forms the ratio of therapeutic agent: SAE-CD is in the range of about 2:1 to about 1:100 on a molar basis, preferably about 1:1 to about 1:20 and more preferably about 2:1 to about 1:10 on a molar basis. See column 11, lines 59-66.

Stella teaches several methods for preparation of the tablet core including dry granulation, wet granulation, hot melt granulation, hot melt extrusion, and compression-grinding-recompression. See column 39, lines 10-20. Stella teaches an example wherein the composition is made by hot melt granulation or extrusion wherein the components in the composition are melted (plasticized) and passed thorough an extruder at a temperature of 60 degrees Celsius or melted at a temperature of 60 degrees Celsius and then sized though a 20 mesh screen to form granules. See example 10. Stella on column 27, lines 30-50 teaches the composition should have a melting point of lower than 150 degrees Celsius.

Although Stella teaches the instant process, Stella does not specifically exemplify the process as applied specifically to the composition disclosed on column 18, lines 27-35

comprising 5% of prednisone; 35% SAE-CD; 50% HPMC (polymeric binder); and lactose (excipient).

However, it would have been obvious to one of ordinary skill in the art at the time the invention was made to look to the guidance provided by Stella et al and utilize a hot melt extrusion/granulation to make the composition disclosed on column 18. One would have been motivated to do so since Stella teaches a variety of methods may be utilized to make the compositions including the instant hot melt extrusion/granulation. Further, Stella exemplifies this technique and thus a skilled artisan would have been motivated to utilize the guidance provided by example 10 and use it to formulate the dosage form disclosed on column 18. Moreover, Stella teaches the melting point of the composition should be lower than 150 degrees Celsius and the melt temperature may be lowered by a plasticizer. Thus, a skilled artisan would have been motivated to maintaining the temperature at 150 degrees Celsius or lower than 150 degrees Celsius.

With regard to claim 2, Stella teaches various ratios of the active to ratio, i.e. about 2:1 to about 1:10 on a molar basis, which lies within the claimed range.

With regard to claims 9 and 10, absent the unexpectedness of mixing the polymer and cyclodextrin prior to mixing the drug, it is the examiner's position that the sequence in which the components are mixed and melted would not effect the process since all the components are rendered in a "plasticized", i.e. melted state. For instance, Stella teaches mixing and melting all the components without specifying the sequence; however the sequence is considered obvious since the critical process of melting all the components is taught.

With regard claim 13, Stella teaches various active ingredients including vitamins and minerals on column 26, lines 20-45. Thus, it would have been obvious to one of ordinary skill in the art at the time the invention was made substitute the exemplified prednisone with the instantly claimed active agents depending on the desired intended use of the composition. For instance, if one desired to formulate a dietary supplement, a skilled artisan would have been motivated to incorporate a vitamin as the active agent of choice.

Claims 3-4 are rejected under 35 U.S.C. 103(a) as being unpatentable over Stella et al (6,046,177) in view Klimesh et al (4880585).

The teachings of Stella et al have been delineated above wherein Stella teaches melt extrusion as a method of making the solid dosage form.

Stella et al do not specify the type of extruder used to shape the solid dosage form.

Klimesh et al teaches a method of continuous tableting. See abstract. Klimesh teaches melt extrusion wherein an extrudable composition is a pharmaceutical are mixtures of one or more pharmaceutical active compounds with one or more auxiliaries conventionally used for the preparation of pharmaceutical tablets; by conversion to a paste with, for example, water at elevated temperatures (not less than 70.degree. C.) or by melting or softening of one or more components, the said mixtures become extrudable. See column 2, lines 40-50. Klimesh teaches the process provides a simple, continuous method of tableting wherein the mixture is extruded and the still deformable extrudate is pressed between two rollers which are driven in opposite directions and possess depressions opposite one another in the roller shell (molding calendar), the form of these depressions determining the tablet shape. Thus, the process eliminates premixing (col. 1, lines 16-27 and 28-34).

It would have been obvious to one of ordinary skill in the art at the time the invention was made to combine the teachings of Stella et al and Klimesh et al and utilize a molding calendar in the extrusion process. One would be motivated to do so since Klimesh et al teach the advantages using mold calendaring to make solid dosage forms via a simple process and eliminating the step of premixing.

Claims 2-18 are rejected under 35 U.S.C. 103(a) as being unpatentable over Baert et al (6,365,188) in view of Stella et al (6,046,177).

Baert et al teach a solid mixture of cyclodextrin prepared via melt extrusion. The melt-extrusion mixture contains cyclodextrin and an active agent. See column 3, lines 26-40. Baert discloses that cyclodextrins increase the solubility of the insoluble drugs such as anti-fungals, specifically itraconazole. Any suitable compound may be utilized provided that the drug does not decompose at high temperatures. See column 2, lines 45-60. Baert teaches the use of substituted and unsubstituted cyclodextrins including beat-cyclodextrin, hydroxypropyl-β-cyclodextrin, and sulfobutylcyclodextrins. See column 7 in its entirety and specifically lines 61 and column 8; lines 4-10. Baert teaches melt-extrusion as the polymer extrusion technique wherein an active agent is embedded in one or more carriers. In this technique the active and excipients are molten in the extruder and hence embedded in the thermoplastic and thermomelting polymers. See column 3, lines 26-40. Additionally, the mixture may contain additives such as instant polyethylene glycol. See column 4, lines 34-42. The process includes a) mixing the cyclodextrin with the active agent and additives, b) mixing optional additives, c) heating the mixture until melting of one of the components occurs, d) forcing the mixture through one or more nozzles, and e) cooling the mixture to obtain a solid product. See column 4, lines 15-25. Although, a temperature of 239

degrees Celsius is exemplified, Baert discloses that different temperatures may be applied and discloses the method of ascertaining the required temperature. See column 5, lines 1-12. The extruder has counterotating screw with different shapes. See column 5. The melt-extruded mixture is preferably prepared without water or a solvent. The preferred ratio of the active to cyclodextrin is 1:3. See column 7, lines 64 to column 8, lines 4 and examples.

Baert et al do not specify the optional additives or the weight percent of the optional additives. Additionally, Baert does not teach the instant temperature of 170 degrees Celsius.

Stella et al teaches controlled release forms of solid formulations containing sulfoalkyl ether cyclodextrin (SAE-CD). The controlled release formulation contains a core containing an active agent, at least on SAE-CD, at least one rate controlling modifier, and at least one pharmaceutical acceptable excipient. See column 6, lines 1-7. The core may be made by several methods including melt extrusion. Note example 10. The release rate modifier provides either a delayed, sustained, timed, or targeted release of the active agent. See column 27, lines 40-50. Stella teaches varying the ratio of the rate controlling modifier and the drug such as 10:1 and 5:1, determines the release rate. The rate control modifier (exemplified HPMC) is varied from 25% to 50%. See column 17. Stella et al teach a controlled release device comprising 5% of prednisone; 35% SAE-β-CD; 50% HPMC (modified natural polymeric binder as defined by page 4 of the specification); and 10% lactose (excipient). See column 18, lines 27-35.

Other release rate modifiers include HPMC, HPC, cellulose acetate butyrate, cellulose acetate propionate, cellulose propionate, carrageenan, cellulose acetate, cellulose nitrate, methylcellulose, hydroxyethyl cellulose, ethylcellulose, polyvinyl acetate, latex dispersions, acacia, tragacanth, guar gum, and gelatin. See column 39, lines 10-20.

Further, Stella teaches the use of binders such as celluloses, polyethylene glycols, polyvinylpyrrolidone, vinyl alcohol polymers, in order to obtain suitable products. See column 27, lines 5-30. Some of the binders named also function as the release rate modifier. See column 27, lines 48-50. The binder is utilized in different proportions in different examples. The example on column 37 utilizes 43% of EMDEX (a binder). Example 10 discloses a process utilizing melt extrusion wherein 2.5% of an active, 67.5% of SAE-CD, 10.5% PEG 6000, and excipients are melted at 60 degrees Celsius to form granules.

It would have been obvious at the time the invention was made to combine the teachings of Baert et al and Stella et al and utilize the a polymer as the additive in Baert's process. Firstly, one would have been motivated to do so since Stella teaches the use of a rate controlling modifiers, such as exemplified HPMC, control the release rate of the active to provide for a delayed, targeted, sustained, etc. dosage form. Therefore, one would have been motivated to add a polymer such as instant polymer in the instant amount, to modify the release rate of the dosage form. Further, it would have been obvious to utilize the polymer in the instant weight percent since Stella teaches the concentration of the rate controlling polymer determines the release rate. Therefore, depending on the release rate of the active, a skilled artisan would have been motivated to adjust the concentration accordingly. For instance, if one desired a slow release rate, a skilled artisan would have been motivated to add 50% of the polymer.

With regard to the temperatures, the examiner points out that Baert teaches the use of various cyclodextrin derivates including sulfobutyl cyclodextrins, thus the melt extrusion temperature depends on the type of the cyclodextrin used and the components in the composition itself. Therefore, if one utilized a composition comprising the polymer additive and a sulfoalkyl

ether cyclodextrin, one would have used a temperature such as 60 degrees Celsius as taught by Stella et al. Further, a skilled artisan would have reasonably expected success in the variation of the temperature since Baert teaches that different temperatures may be applied and discloses the method of ascertaining the required temperature.

With regard to claims 9 and 10, absent the unexpectedness of mixing the polymer and cyclodextrin prior to mixing the drug, it is the examiner's position that the sequence in which the components are mixed and melted would not effect the process since all the components are rendered in a "plasticized", i.e. melted state.

With regard to claim 13, Baert teaches the use of any active agent that is not degraded by melt extrusion heat temperatures and agents, which are pharmaceutical and cosmetically used to treat humans. See column 3, lines 15-25. Therefore, it would have been obvious to look to Stella and utilize the instantly claimed active agent depending on the desired intended use of the solid dosage form. If one desired providing a dietary supplement, one would have used minerals taught by Stella on column 26, lines 20-45, as the active agent.

Response to Arguments

Applicant argues that claim 8 was not rejected and claims 2-7 have been amended to depend on claim 8. Thus, the rejection is rendered moot.

Applicant's arguments filed 8/24/06 have been fully considered but they are not persuasive. Firstly, the examiner points out that cancelled claim 1 which required 15-98% of a specific binder selected from PEG with a molecular weight of 4000, PVP, or copolymers comprising N-vinylpyrollidone and vinyl acetate. Stella only taught about 10.5% of the claimed binder, PEG with the claimed molecular weight of 6000; thus the examiner could not reasonably

reject dependent claim 8, which required 50-98% of the specific binders recited in a Markush group. However, applicant has cancelled claim 1 and has amended claim 8 to be an independent claim. Claim 8 as amended only requires 50-98% of *at least one* polymeric binder without specifying the binder. Thus, claim 8 is broader since cancelled claim 1 required a specific binder from a Markush group. Thus, the examiner has rejected claim 8 since Stella teaches 50% of HPMC (note this is defined as a polymeric binder in the instant specification on page). It should be also noted that claim 8 is broad for the cyclodextrin, which provides the examiner further motivation to look to Stella. As set forth in the above rejection, Stella teaches the use of SAE-cyclodextrins which can be melt extruded at 60 degrees Celsius and Baert teaches the use of various cyclodextrins such as sulfobutyl cyclodextrins. Therefore, depending on the cyclodextrin utilized, the melting point of the entire composition changes. Thus, the examiner retains the right to go final since the amendment to claim 8 necessitated the new rejection.

Applicant argues that Baert does not teach the instant temperature of less than 170 degrees Celsius and Baert does not teach 50-98% polymeric binder. Applicant argues that the use of a secondary reference is improper hindsight. Although Baert teaches the temperature needs to be the melting point of the of one or more of the cyclodextrins or the active agent Applicant argues that the examiner cannot broaden the meaning of "one or more components" to include other materials such as the binder since it would be impermissible hindsight. Applicant argues that although Baert teaches the use of optional additives in the composition, Baert only mentions antioxidants, pigments, flavors, and plasticizers. However, Baert does not teach the instant weight percent of 50-98%. Applicant argues that Baert was aware of the melt extrusion process and still did not teach the polymeric binder.

In response to applicant's argument that the examiner's conclusion of obviousness is based upon improper hindsight reasoning, it must be recognized that any judgment on obviousness is in a sense necessarily a reconstruction based upon hindsight reasoning. But so long as it takes into account only knowledge which was within the level of ordinary skill at the time the claimed invention was made, and does not include knowledge gleaned only from the applicant's disclosure, such a reconstruction is proper. See *In re McLaughlin*, 443 F.2d 1392, 170 USPQ 209 (CCPA 1971). In instant case, Baert teaches the use of any suitable additive. Although Baert does not teach the instant additive, it is clear that any pharmaceutically acceptable additive may be used. Thus, the inclusion of an additive in the melt extrusion composition is not hindsight reasoning since this is clearly taught by Baert. The secondary reference, Stella, teaches the use of release rate modifying polymers in a composition comprising cyclodextrin and an active agent. The purpose of the polymer is to manipulate the release rate wherein a higher concentration (50%) slows the release rate and a lower concentration provides faster release. Further, Stella teaches the dosage form may be made by melt extrusion wherein a temperature of 60 degrees Celsius is used. Thus, the melt extrusion temperature would vary according to the components in the composition. Although Baert exemplifies a temperature of 239 degrees Celsius, Baert discloses that different temperatures may be applied depending on the composition and discloses the method of ascertaining the required temperature. Clearly, the temperature exemplified by Baert is not critical since as taught by Baert, it depends on the components in the composition. Thus, the manipulation of the temperature is not hindsight reasoning since the reference itself teaches the manipulation of the temperature as discussed above. Moreover, applicant argues that the temperature taught by Baert must melt either the

cyclodextrin or the active agent. The examiner points out that the preferred drug, itraconazole, has a melting temperature of 166.2 degrees Celsius and as argued by applicant, Baert teaches a temperature must melt either the cyclodextrin or the active agent. Thus, clearly a temperature of less than 170 degrees Celsius would be suitable. Furthermore, the examiner points out that Baert teaches the use of various cyclodextrins including sulfoalkyl cyclodextrins. The examiner points out that depending on the type of cyclodextrin used, the melt extrusion temperature would also change. Thus, if one used a sulfoalkyl-cyclodextrin, then one would use the melt extrusion temperature taught by Stella et al, which is 60 degrees Celsius.

Therefore it is the examiner's position that the instant claims are prima facie obvious for the reasons discussed above.

The rejection of claims 1-8 under 35 U.S.C. 103(a) as being unpatentable over Baert et al (6,365,188) in view of Goertz et al (4,801,460) is withdrawn.

Conclusion

Claims 2-18 are rejected.

Applicant's amendment necessitated the new ground(s) of rejection presented in this Office action. Accordingly, **THIS ACTION IS MADE FINAL**. See MPEP § 706.07(a). Applicant is reminded of the extension of time policy as set forth in 37 CFR 1.136(a).

A shortened statutory period for reply to this final action is set to expire THREE MONTHS from the mailing date of this action. In the event a first reply is filed within TWO MONTHS of the mailing date of this final action and the advisory action is not mailed until after the end of the THREE-MONTH shortened statutory period, then the shortened statutory period will expire on the date the advisory action is mailed, and any extension fee pursuant to 37

CFR 1.136(a) will be calculated from the mailing date of the advisory action. In no event, however, will the statutory period for reply expire later than SIX MONTHS from the date of this final action.

Any inquiry concerning this communication or earlier communications from the examiner should be directed to Sharmila S. Gollamudi whose telephone number is 571-272-0614. The examiner can normally be reached on M-F (8:00-5:30), alternate Fridays off.

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Johann Richter can be reached on 571-272-0646. The fax phone number for the organization where this application or proceeding is assigned is 571-273-8300.

Information regarding the status of an application may be obtained from the Patent Application Information Retrieval (PAIR) system. Status information for published applications may be obtained from either Private PAIR or Public PAIR. Status information for unpublished applications is available through Private PAIR only. For more information about the PAIR system, see http://pair-direct.uspto.gov. Should you have questions on access to the Private PAIR system, contact the Electronic Business Center (EBC) at 866-217-9197 (toll-free). If you would like assistance from a USPTO Customer Service Representative or access to the automated information system, call 800-786-9199 (IN USA OR CANADA) or 571-272-1000.

Sharmila S. Gollamudi
Examiner
Art Unit 1616